REMARKS

Claims 1-34 are pending in the present application. In the outstanding Official Action, the Examiner has required restriction to the following inventions under 35 U.S.C. §121 and 372, as follows:

Group I: Claims 1-8 drawn to a fluorescent probe for real-time detection of amplification of nucleic acid, wherein a fluorescent dye of which intensity of fluorescence is varied when the dye is intercalated into a double-stranded nucleic acid, is connected with an oligonucleotide of which base sequence is complementary with at least a part of said nucleic acid.

Group II: Claims 9-21 drawn to a real-time detection method of nucleic acid amplification, comprising the steps of:
i) producing an aqueous buffer which contains a nucleic acid, a pair of primers for amplification of said nucleic acid, a fluorescent probe wherein a fluorescent dye of which intensity of fluorescence is varied when the dye is intercalated into a double-stranded nucleic acid, is connected with an oligonucleotide of which base sequence is complementary with at least a part of said nucleic acid, four (4) kinds of nucleotides and DNA polymerase;
ii) denaturing said double-stranded nucleic acid into single strands by heating the aqueous buffer prepared in step i) up to 93 °C to 96 °C;
iii) annealing said pair of primers with said single strand by cooling the solution obtained in step ii) up to 50 °C to 57 °C;
iv) replicating said single-stranded nucleic acid by heating the solution obtained from step iii) up to 70 °C to 74 °C;
v) denaturing said replicated nucleic acid into single strands by heating the solution obtained in step iv) up to 93 °C to 96 °C;
vi) annealing said fluorescent probe with said single-stranded nucleic acid by cooling the solution obtained in step v) up to 50 °C to 57 °C;
vii) measuring an intensity of the fluorescence emitted from the solution obtained in step vi); and
viii) repeating more than one steps iv) through vii).

Group III: Claims 22-36 drawn to a real-time detection method of the nucleic acid amplification, comprising the steps of
i) producing an aqueous buffer which contains a nucleic acid, a pair of primers for amplification of said nucleic acid, a primer for reverse transcription, a fluorescent probe wherein a fluorescent dye of which intensity of fluorescence is varied when the dye is intercalated into a double-stranded nucleic acid, is connected with an oligonucleotide of which base sequence is complementary with at least a part of said nucleic acid,

four(4) kinds of nucleotides, DNA polymerase and reverse transcriptase;
ii) replicating a single-stranded cDNA by heating the aqueous buffer prepared in step i) up to 42 °C to 50 °C;
iii) denaturing a primer for a reverse transcription and a reverse transcriptase from said single-stranded cDNA by heating the solution obtained from said step ii) up to 93 °C to 96 °C;
iv) annealing the pair of primers with said single-stranded nucleic acid by cooling the solution obtained from said step iii) up to 50 °C to 57 °C;
v) replicating said single-stranded nucleic acid by heating the solution obtained from step iv) up to 70 °C to 74 °O;
vi) denaturing said replicated nucleic acid into single strands by heating the solution obtained from step v) up to 93 °C to 96 °C;
vii) annealing said fluorescent probe with said single-strand nucleic acid by cooling the solution obtained from step vi) up to 50-57 °C;
viii) measuring an intensity of the fluorescence emitted from the solution obtained in step vii); and
ix) repeating more than one steps v) through viii).

The Examiner has also required election of a single sequence from the sequences with SEQ ID NO: 1-22 recited in claims 8, 20 and 33.

Applicants initially note that claims 22-36 as above in Group III, should be claims 22-34 since only claims 1-34 are pending in the present application.

PROVISIONAL ELECTION

Applicants provisionally elect Group I of claims 1-8 drawn to a fluorescent probe for real-time detection of amplification of nucleic acid as recited in present claim 1, for prosecution on the merits, with traverse.

Further, Applicants provisionally elect the sequence with SEQ ID NO: 16, with traverse. As required by the Examiner, Applicants submit that claims 1-34 read upon the elected species.

Applicants note that upon allowance of a generic claim, Applicants will be entitled

to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 C.F.R. §1.141. Applicants reserve the right to file a divisional application directed to the non-elected subject matter.

TRAVERSAL

Applicants respectfully traverse this restriction/election requirement because Groups I-III share a ***special technical feature*** under PCT Rule 13.2, and thus, all of the presently pending claims possess unity of invention. Accordingly, restriction is improper.

PCT Rule 13.2 states the following, in relevant part:

> "[T]he requirement of unity of invention referred to in Rule 13.1 shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression 'special technical features' shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art."

In the present application, the special technical feature that is shared between Groups I-III is a "fluorescent probe for real-time detection of amplification of nucleic acid wherein a fluorescent dye of which intensity of fluorescence is varied when the dye is intercalated into a double-stranded nucleic acid, is connected with an oligonucleotide of which base sequence is complementary with at least a part of said nucleic acid." Such a special technical feature of the present invention is novel and superior to the nucleic acid probe disclosed in *Mergny et al.* which the Examiner cited in the Official Action, thereby contributing to the prior art as a whole.

In view of the foregoing, Applicants respectfully submit that the claims of Groups

I-III possess "unity of invention" because they share a special technical feature as required by PCT Rule 13.2. Thus, restriction of the claims of Groups I-III is improper. Accordingly, the Examiner is respectfully requested to reconsider and withdraw this restriction requirement.

Applicants further submit that the claims of all of Groups I-III should be examined together because, in addition to being improper on the basis of unity of invention, the restriction requirement is further traversed because it omits "an appropriate explanation" as to the existence of a "serious burden" if a restriction were not required between the claims. *See* MPEP § 803. A complete and thorough search for the inventions set forth in the Official Action would be coextensive. Thus, it would ***not*** be a ***serious*** burden upon the Examiner to examine all of the claims in this application.

Furthermore, Applicants have paid a filing fee for an examination of all the claims in this application. If the Examiner refuses to examine the claims paid for when filing this application and persists in requiring Applicants to file divisional applications for each of the groups of claims, the Examiner would essentially be forcing Applicants to pay duplicative fees for the non-elected or withdrawn claims, inasmuch as the original filing fees for the claims (which would be later prosecuted in divisional applications) are not refundable.

Applicants assert that the election of species requirement is improper because the species are so linked as to form a single general inventive concept under PCT Rule 13.1 and because the Examiner has provided no reasoning as to why the asserted species are independent or distinct. That is, the Examiner has neither suggested an example of a

separate utility nor has shown separate classification, status, or field of search. Applicants submit that the sequences with SEQ ID NO: 1-22 are so linked as to form a single general inventive concept and should be examined together in the present application. In particular, for example, the sequences with SEQ ID NO: 8-17, 21 and 22 among the sequences with SEQ ID NO: 1-22 in claim 8 have a common property and/or activity: they can be connected with a fluorescent dye and designed based on the same gene sequence (Mycobacterium tuberculosis rpoB). Accordingly, the sequences with SEQ ID NO: 8-17, 21 and 22 may be used for detecting (Mycobacterium tuberculosis rpoB) gene amplication without any difficulties.

Further, the Examiner has not established that a "serious burden" exists. Applicants assert that a complete and thorough search of the subject matter described in the provisionally elected species set forth above would require searching the art areas appropriate to all other subject matter contained in this application. Since a search of the subject matter of the provisionally elected species and all other subject matter contained in this application would be coextensive, it would ***not*** be a ***serious*** burden upon the Examiner to conduct a search of all subject matter contained in this application.

CONCLUSION

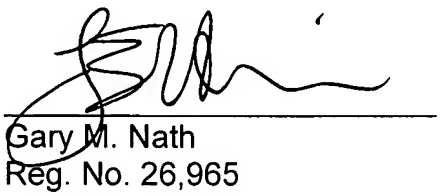
In view of the foregoing, Applicants respectfully request the Examiner to reconsider and withdraw the restriction/election requirement, and to examine all of the claims pending in this application.

If the Examiner has any questions or wishes to discuss this matter, the Examiner is welcomed to telephone the undersigned attorney.

In the event this paper is not timely filed, Applicants petition for an appropriate extension of time. Please charge any fee deficiency or credit any overpayment to Deposit Account No. 14-0112.

Respectfully submitted,

THE NATH LAW GROUP



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